

myoinositol-1,2-cyclic phosphodiester (Dawson *et al.*, 1971) and cyclic lysophosphatidic acid (Friedman *et al.*, 1996).

Except for cyclic AMP and cyclic GMP, which have been extensively studied, no specific biological activities have been so far assigned to the other 5 biological cyclic phosphates.

Breast cancer cells in their virulent undifferentiated state are characterized by lack of functional estrogen and/or progesterone receptors. To date, no method for *in situ* differentiation of breast cancer cells has yet been proven effective in patients.

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GLOSSARY

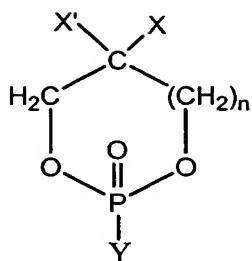
The following is an explanation of some terms used above and in the following description and claims:

15 **CPP** – the 1,3-cyclic propandiol phosphates derivatives used in the present invention.

Target cells – any cells, which have the potential to mature into neural cells. Non-limiting examples of such cells are MCF-7 and T47D human breast cancer 20 cells.

Substantially maintaining - this term relates to the capability of analogs to promote the activity carried out by the cyclic glycerophosphate from which they were derived to a certain extent. The analog's activity will be considered to be 25 substantially maintained wherein the activity is 30% or above, preferably 50% or above, more preferably 70% or above, and most preferably 90% or above the level of the activity of the cyclic glycerophosphate.

Effective amount – wherein the method of the invention is intended for 30 prevention of a non-desired condition, the term “*effective amount*” should then be



or pharmaceutically acceptable salts thereof,

wherein

n is 0 or 1;

5 X is hydrogen, O-R, NH-R or N-(C=O)-R;

X' is hydrogen or CH₂OH;

Y is O-R₁, NH-R₁;

R is hydrogen, linear or branched alkyl, linear or branched acyl, substituted or non-substituted aryl or aralkyl residue;

10 R₁ is hydrogen, linear or branched alkyl, linear or branched acyl, substituted or non-substituted aryl, alkylcarboxy ester or alkyl-N-R₂R₃;

R₂ and R₃ are independently hydrogen or an alkyl group;

provided that when X and X' are hydrogen and n=0, Y is not O-R₁ wherein R₁ is hydrogen, alkyl or aryl; and provided that when X' is CH₂OH then X is NH-R or

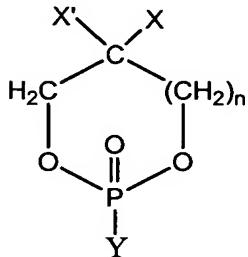
15 NO₂.

As used herein the term "*alkyl*" refers to an alkyl group having from 1 to 24 carbon atoms, e.g. preferably from 3 carbon atoms to 20 carbon atoms, most preferably from 5 carbon atoms to 15 carbon atoms; the term "*acyl*" refers to an aliphatic saturated or unsaturated C₁ - C₂₄ acyl group, preferably an acyl group

20 having an even number of carbon atoms, most preferably an acyl group derived from a natural fatty acid such as a saturated aliphatic acyl group selected from acetyl, butyryl, caproyl, octanoyl, decanoyl, lauroyl, myristyl, palmitoyl and stearoyl, or an unsaturated aliphatic acyl group selected from palmitoleyl, oleyl, linoleyl, and ricinoleyl; and the term "*aryl*" refers to a mono- or poly-carbocyclic

CLAIMS:

1. A compound of the following formula I:



5 or pharmaceutically acceptable salts thereof,

wherein:

n is 0 or 1;

X is hydrogen, O-R, NH-R or N-(C=O)-R;

X' is hydrogen or CH₂OH;

10 Y is O-R₁, NH-R₁;

R is hydrogen, linear or branched alkyl, linear or branched acyl, substituted or non-substituted aryl or aralkyl residue;

R₁ is hydrogen, linear or branched alkyl, linear or branched acyl, substituted or non-substituted aryl, alkylcarboxy ester or alkyl-N-R₂R₃;

15 R₂ and R₃ are independently hydrogen or an alkyl group;

alkyl is an alkyl group having from 1 to 24 carbon atoms, preferably from 3 carbon atoms to 20 carbon atoms, most preferably from 5 carbon atoms to 15 carbon atoms;

acyl is an aliphatic saturated or unsaturated C₁ - C₂₄ acyl group, preferably an acyl

20 group having an even number of carbon atoms, and most preferably an acyl group derived from a natural fatty acid such as a saturated aliphatic acyl group or an unsaturated aliphatic acyl group;

aryl is a mono- or poly-carbocyclic aryl group, most preferably phenyl, optionally substituted by C₁ - C₄ alkyl, halogen and/or hydroxy;

provided that when X and X' are hydrogen and n=0, Y is not O-R₁ wherein R₁ is hydrogen, alkyl or aryl; and provided that when X' is CH₂OH then X is NH-R or NO₂.

2. A compound according to claim 1, wherein the acyl moiety is selected
5 from the group comprising of acetyl, butyryl, caproyl, octanoyl, decanoyl, lauroyl, myristyl, palmitoyl and stearoyl, palmitoleyl, oleyl, linoleyl, and ricinoleyl.

3. A compound according to claim 1 wherein Y is OH and X is O-R or NH-R; wherein R is a linear or branched alkyl or linear or branched acyl.

4. A compound according to claim 1 wherein X is hydrogen and Y is O-acyl
10 or NH-R₁; wherein R₁ is a linear or branched alkyl or linear or branched acyl.

5. Compounds of formula I according to claim 1 selected from the group consisting of:

(a) 1,3-cyclic propandiol phosphate-5-oleoyl;

(b) 1,3-cyclic propandiol phosphate-5- benzyloxy;

15 (c) 1,3-cyclic propandiol phosphate-5- benzylamino;

(d) 1,3-cyclic propandiol phosphate-5- caproylamido;

(e) 1,3-cyclic propandiol phosphate-2-benzyloxy;

(f) 1,3-cyclic propandiol phosphate-2- acetoxy;

(g) 1,3-cyclic propandiol phosphate-2-methylamino;

20 (h) 1,3-cyclic propandiol phosphate-5-glycine ethylester;

(i) 2-methyl 1,3-cyclic propanediol phosphate;

(Ten) 1-methyl 1,3-cyclic propanediol phosphate;

(Eleven) 2-dimethylamine ethyl ester 1,3-cyclic propanediol phosphate;

(Twelve) 1,3-cyclic propanediol phosphoamidate;

(Thirteen) 1,3-cyclic propanediol N-ethyl phosphoamidate;

(Fourteen) 1,3-cyclic propanediol phosphoamidate glycine ethylester;

(Fifteen) 2-benzyloxy 1,3-chloropropanediol phosphate;

(Sixteen) 2-caproimido 1,3-chloropropanediol phosphate;

(Seventeen) 5-amino-5-hydroxymethyl-2-oxo-2λ5-[1,3,2]dioxaphosphinan-2-

30 ol;

(Eighteen) 5-nitro-5-hydroxymethyl-2-oxo-2λ5-[1,3,2]dioxaphosphinan-2-ol;
or pharmaceutically acceptable salts thereof.

6. A pharmaceutical composition comprising a pharmaceutical acceptable carrier and, as an active ingredient, a compound of the general Formula I in Claim
5 1 or pharmaceutically acceptable salt thereof.

7. A pharmaceutical composition according to claim 6, for promoting cell differentiation in cancerous cells.

8. A pharmaceutical composition according to claim 6, for promoting protein expression in cancerous cells.

10 9. A pharmaceutical composition according to claim 8, wherein said protein is estrogen receptor - α or progesterone receptor.

10. A pharmaceutical composition according to any one of claims 6 to 9 wherein the compound of formula I is selected from the group consisting of

(a) 1,3-cyclic propandiol phosphate-5-oleoyl;

15 (b) 1,3-cyclic propandiol phosphate-5- benzyloxy;

(c) 1,3-cyclic propandiol phosphate-5- benzylamino;

(d) 1,3-cyclic propandiol phosphate-5- caproylamido;

(e) 1,3-cyclic propandiol phosphate-2-benzyloxy;

(f) 1,3-cyclic propandiol phosphate-2- acetoxy;

20 (g) 1,3-cyclic propandiol phosphate-2-methylamino;

(h) 1,3-cyclic propandiol phosphate-5-glycine ethylester;

(i) 2-methyl 1,3-cyclic propanediol phosphate;

(Ten) 1-methyl 1,3-cyclic propanediol phosphate;

(Eleven) 2-dimethylamine ethyl ester 1,3-cyclic propanediol phosphate;

26(Twelve) 1,3-cyclic propanediol phosphoamidate;

(Thirteen) 1,3-cyclic propanediol N-ethyl phosphoamidate;

(Fourteen) 1,3-cyclic propanediol phosphoamidate glycine ethylester;

(Fifteen) 2-benzyloxy 1,3-chloropropanediol phosphate;

(Sixteen) 2-caproimido 1,3-chloropropanediol phosphate;

(Nineteen) 5-amino-5-hydroxymethyl-2-oxo-2λ5-[1,3,2]dioxaphosphinan-2-ol;

(Ten) 5-nitro-5-hydroxymethyl-2-oxo-2λ5-[1,3,2]dioxaphosphinan-2-ol;
or pharmaceutically acceptable salts thereof.

- 5 11. Use of a compound of formula I for the preparation of a medicament for treating disorders and diseases, which can be treated by promoting cell differentiation, substantially as described in the specification.
12. Use according to claim 11, wherein said disorder is tumor growth.
13. Use of a compound of formula I for the preparation of a medicament for 10 treating disorders and diseases, which can be treated by promoting protein expression, substantially as described in the specification.
14. Use according to claim 13, wherein said protein is estrogen receptor- α or progesterone receptor.

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